# A case of Powassan encephalitis acquired in southern Quebec

Mark Sanderson MD, L. Robbin Lindsay PhD, T. Mark Campbell MD MSc, Muhammad Morshed PhD

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A 68-year-old woman presented to the emergency department in Kelowna, British Columbia, with a 3-day history of fever, fatigue, weakness, confusion, headache and diplopia. On initial assessment, she was febrile (38.8°C), and a screening neurologic examination showed a right cranial sixth nerve palsy and mild left-sided pyramidal weakness. The patient had a small erythematous mark on her right shoulder, but no target lesion. She was on vacation from the Ottawa region of Ontario and had been previously well. Her medical history was unremarkable.

Three weeks prior, she had been vacationing in the Luskville region of the province of Quebec. On her return home, a tick was discovered attached to her right shoulder, removed and sent to a Public Health Ontario laboratory for analysis. The patient was well at that time and was given a single prophylactic dose of doxycycline (the standard prophylactic dose is 200 mg) by her primary care physician for Lyme disease. Three days later, the patient travelled to Nanaimo, BC, via Vancouver, and later that week to Kelowna, BC, where she became symptomatic.

Initial complete blood count, basic electrolytes and hepatic studies were normal, whereas a lumbar puncture showed an inflammatory cerebrospinal fluid with leukocytosis and mild protein elevation (Box 1). Magnetic resonance imaging (MRI) of the brain showed nonspecific, mild hyperintensities in the supratentorial white matter on $T_2$-weighted and fluid-attenuated inversion recovery (FLAIR) sequences.

Empiric antimicrobial therapy for meningoencephalitis was instituted with vancomycin 1000 mg intravenously (IV) every 8 hours (1500 mg IV loading dose), ceftriaxone 2000 mg IV every 12 hours, piperacillin–tazobactam 3.375 g IV every 6 hours, doxycycline 100 mg orally twice daily and acyclovir 600 mg IV every 8 hours.

During her admission, the patient's condition deteriorated, and she developed bilateral sixth nerve palsies, a left facial droop, dysarthria, and worsening weakness disproportionately affecting the upper extremities. She was transferred to the intensive care unit and began to improve 5 days after admission.

Initial microbiologic investigations were negative for Powassan virus and other common infectious causes of encephalitis (Box 1). The National Microbiology Laboratory in Winnipeg confirmed the tick to be a partially engorged nymphal *Ixodes marxi,* a species known to be a vector of Powassan virus. Molecular testing of RNA extracted from the submitted tick was positive for Powassan virus, lineage 1. Further testing for Powassan virus and western equine encephalitis virus on cerebrospinal fluid and convalescent sera collected 1 week later was also negative. Because the tick retrieved from the patient was strongly positive for Powassan virus by nucleic acid test, and because she also presented with classic symptoms of Powassan encephalitis, antibiotic and antiviral therapies were discontinued and the patient was given supportive therapy.

Confirmatory testing was performed on the patient's sera by the Centers for Disease Control and Prevention in Fort Collins, Colorado. Both hemagglutination inhibition testing and gold standard plaque reduction neutralization testing were strongly positive, with a greater than fourfold increase in reduction neutralization testing between initial (day 0) and convalescent (day 8) serological assays, confirming the diagnosis (Box 1).

At 3-month follow-up, the patient had completed 7 weeks of intensive inpatient multidisciplinary rehabilitation; she showed good functional recovery of her lower extremities, with improvement in function of the right upper extremity. She continued to show mild residual dysphagia, mild left-facial weakness and substantial flaccid weakness in the left upper extremity. Because of concerns about possible lower motor neuron involvement, the patient was referred for electrodiagnostic testing. Motor and sensory nerve conduction studies were within normal limits; however, there was evidence of diffuse denervation and reinnervation across multiple myotomes. This was interpreted as being most consistent with

## KEY POINTS

- Powassan virus is an arbovirus that is an uncommon but increasingly recognized cause of infection-related encephalitis in Canada.
- Traditional ranges of *Ixodes* ticks are expanding, and the incidence of Powassan virus is growing.
- Lack of a known tick exposure should not rule out Powassan encephalitis when there is strong clinical suspicion.
- Early negative results from serum and cerebrospinal fluid studies do not rule out Powassan encephalitis, and testing of acute and convalescent serum samples by hemagglutination inhibition or plaque reduction neutralization testing should be undertaken if suspicion is high.
- In the acute phase, treatment is mainly supportive; rehabilitation is often required, as recovery outcomes range from mild to severe disability.

**Box 1: Test results in a 68-year-old woman with Powassan encephalitis**

| Test | Result (reference range)* |
|---|---|
| Hemoglobin, g/L | 124 (118–151) |
| Mean corpuscular volume, fL | 89.0 (84.0–98.0)) |
| Platelet count, x $10^9$/L | 185 (147–375) |
| Leukocyte count, x $10^9$/L | 8.6 (3.1–9.7) |
| Absolute neutrophil count, x $10^9$/L | 6.5 (1.2–6.0) |
| Lymphocyte count, x $10^9$/L | 0.9 (0.6–3.1) |
| Monocyte count, x $10^9$/L | 1.1 (0.2–0.9) |
| Cerebrospinal fluid leukocyte count, x $10^6$/L | 31 (0–5) |
| Cerebrospinal fluid lymphocytes, % | 89 |
| Cerebrospinal fluid glucose, mmol/L | 3.0 (2.2–3.9) |
| Cerebrospinal fluid protein, g/L | 1.05 (0.12–0.60) |
| Herpes simplex virus nucleic acid test | Negative |
| Varicella–zoster virus nucleic acid test | Negative |
| Enterovirus nucleic acid test | Negative |
| Mumps nucleic acid test | Negative |
| Measles nucleic acid test | Negative |
| *Coxiella burnetii* antibody test | Negative |
| *Rickettsia rickettsii* antibody test | Negative |
| West Nile virus nucleic acid test, IgM, IgG | Negative, negative, negative |
| Cytomegalovirus IgM, IgG | Negative, negative |
| Epstein–Barr virus IgM, IgG | Negative, negative |
| *Bartonella henselae* antibody test | Negative |
| *Borrelia burgdorferi* antibody test | Negative |
| *Treponema pallidum* antibody test | Negative |
| Powassan virus hemagglutination inhibition test | |
| Convalescent (day 30) | Positive at 1:160 |
| Powassan virus plaque reduction neutralization test | |
| Initial (day 0) | Positive at 1:320 |
| Convalescent (day 8) | Positive at 1:5120 |

Note: IgG = immunoglobulin G, IgM = immunoglobulin M.
*If applicable.

motor neuronopathy. Results from cognitive evaluation were within normal limits, and 3-month follow-up MRI of the brain was unchanged from previous imaging.

## Discussion

Powassan encephalitis is a known, but rare, consequence of infection by Powassan virus, an arbovirus within the genus *Flavivirus*, closely related to West Nile, dengue, yellow fever and Zika viruses. Powassan virus is likely an underrecognized cause of encephalitis. Powassan virus was first described in 1958 by McLean and Donohue; they isolated the virus from the brain of a boy from Powassan, Ontario, who died of encephalitis.[1]

The clinical literature is largely limited to case reports and case series of the disease. This virus is found in temperate regions in parts of Canada, the United States and Russia.[2] In North America, Powassan virus exists in 2 genetically distinct lineages, Powassan virus lineage I and deer tick virus (Powassan virus lineage II), and is maintained within 3 distinct transmission cycles among tick vectors and mammalian reservoirs (Box 2).[1,2] In most reports, a definitive history of tick bites is lacking, but exposure to tick-endemic regions or outdoor activities is often reported. Unlike many other tick-borne pathogens that require an extended period of tick feeding before transmission occurs, Powassan virus rapidly disseminates from the tick vector to its host. *Ixodes scapularis* ticks were shown in an in vivo study to transmit Powassan virus lineage II to mice after as little as 15 minutes of attachment and feeding.[3]

The incidence of Powassan encephalitis in the US has increased in recent years, especially in the Midwest; this is likely due in part to increased surveillance and recognition, along with higher prevalence in blacklegged ticks and broader geographic distribution of infected tick populations.[4,5] In Canada, most cases of Powassan virus have been associated with the prototypical lineage I (as is reported here), which remains a rare infection with cases limited to eastern Canada.[6] Antibodies to Powassan virus have been detected in historical serologic surveys of humans from the western provinces of BC and Alberta,[2] thus the scope of risk of human exposure in western North America remains to be defined. Although cases of infection with the deer tick virus lineage of Powassan virus are rare in Canada, this lineage has been detected in small numbers of blacklegged ticks in Manitoba, Ontario and Nova Scotia (R.L., unpublished data, 2017), and this tick species has expanded its range extensively in much of central and eastern Canada.

**Box 2: Arthropod vectors, animal reservoirs and associated Powassan virus lineage[1,2]**

| Vector | Reservoir | Lineage |
|---|---|---|
| *Ixodes cookei* | Groundhogs, skunks | Powassan virus lineage I |
| *Ixodes marxi* | Squirrels | Powassan virus lineage I |
| *Ixodes scapularis* | White-footed mice, deer mice | Powassan virus lineage II (deer tick virus) |
| *Ixodes spinipalpis* | Unconfirmed | Unspecified* |
| *Dermacentor andersoni* | Unconfirmed | Powassan virus lineage I |

*The lineage of Powassan virus transmitted by *Ixodes spinipalpis* is not known.

## Clinical features and diagnosis

Typical symptoms of Powassan encephalitis are nonspecific and include fever, headache, nausea, vomiting, lethargy, weakness and confusion.[1,7,8] Less common presentations can include findings of meningitis, encephalitis, seizures, cranial nerve abnormalities and coma.[1] The virus has an incubation period of 8 to 34 days.[7] Since the discovery of this pathogen, about 100 cases have been found in North America, and limited information is available on the diagnosis of Powassan virus. Serology (hemagglutination inhibition) is the main mode of diagnosis. Initial blood samples should be collected when the patient is acutely ill. However, a second set of blood samples may need to be collected about 2 weeks later, as the initial samples are often negative, as in this case. We suggest that convalescent samples be tested at least 4 weeks after the date of symptom onset.

Laboratory findings are nonspecific in cases of Powassan encephalitis, and patients may have normal results on screening blood tests. Cerebrospinal fluid investigations may yield a normal glucose level, a normal or slightly elevated protein level, and a leukocytic pleocytosis.[8] Computed tomography of the brain has not been shown to be sensitive enough to detect any changes in patients with Powassan encephalitis.[1] Case reports documenting MRI of the brain have noted changes similar to microvascular ischemia, demyelinating processes, preferential effects on grey matter structures, scattered hyperintensities on $T_2$-weighted and FLAIR sequences, or unremarkable findings.[1,4,7,8] Similar to other arboviruses, electrodiagnostic testing may show evidence of anterior horn cell neuronopathy, which carries a poor prognosis.[9]

## Treatment

Treatment of Powassan encephalitis is supportive, and there are no specific interventions that are recommended.[1,8] Patients may require mechanical ventilation and transfer to a higher level of care owing to progressive weakness and respiratory failure. Expert consultation should be sought early if there are concerns about Powassan encephalitis. The case fatality rate of Powassan encephalitis has been reported to be as high as 10%–15%, with up to 50% of patients suffering long-term neurologic sequelae.[1,7]

Rehabilitation focuses on the neurologic deficits, which may include both central and peripheral nerve pathology.[1] Reduced endurance, poor trunk control, and muscle weakness in the lower extremities must be addressed for the patient to regain ambulation. Purposeful upper-extremity activities are helpful in conjunction with targeted strengthening exercises for regaining function. Screening of cognition and language should be performed, and therapy instituted for identified deficits. Long-term outcomes for encephalitis-related neurologic deficits are variable and may range from rapid and complete resolution to prolonged and incomplete recovery.[10]

## Conclusion

The relatively rare and geographically stable prototypic Powassan virus and the emerging and geographically expanding deer tick virus lineage of Powassan virus are both important pathogens capable of causing encephalitis. Nonspecific symptoms, lack of clinician familiarity with the condition, and poor recognition or recall of tick bites may frustrate accurate diagnosis. Neurologic sequelae may be profound, and recovery is variable. Continued range expansion of blacklegged tick populations and increased prevalence of deer tick virus lineage within infected tick populations will likely mean that the risk of human exposure and the geographic range over which this risk occurs will continue to increase. Primary prevention through public awareness of endemic areas and protection strategies for avoiding tick bites (www.canada.ca/en/public-health/services/diseases/powassan-virus/prevention.html) are the best lines of defence against this disease.

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**Affiliations:** Kelowna General Hospital (Sanderson), Kelowna, BC; University of British Columbia (Sanderson), Vancouver, BC; National Microbiology Laboratory (Lindsay), Public Health Agency of Canada, Winnipeg, Man.; Physical Medicine and Rehabilitation (Campbell), Élisabeth Bruyère Hospital, Ottawa, Ont.; BC Centre for Disease Control Public Health Laboratory (Morshed), Vancouver, BC



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**Correspondence to:** Mark Sanderson, mark.sanderson@alumni.ubc.ca